Tetrahedron Letters No. 39, pp 3413 - 3416, 1977. Pergamon Press. Printed in Great Britain.

# SYNTHESIS OF THIOPHENES FROM ACETYLENES AND BIS-AMINE DISULFIDES

Francisco M. Benitez and John R. Grunwell*

Department of Chemistry, Miami University
Oxford, Ohio 45056

(Received in USA 13 June 1977; received in UK for publication 9 August 1977)

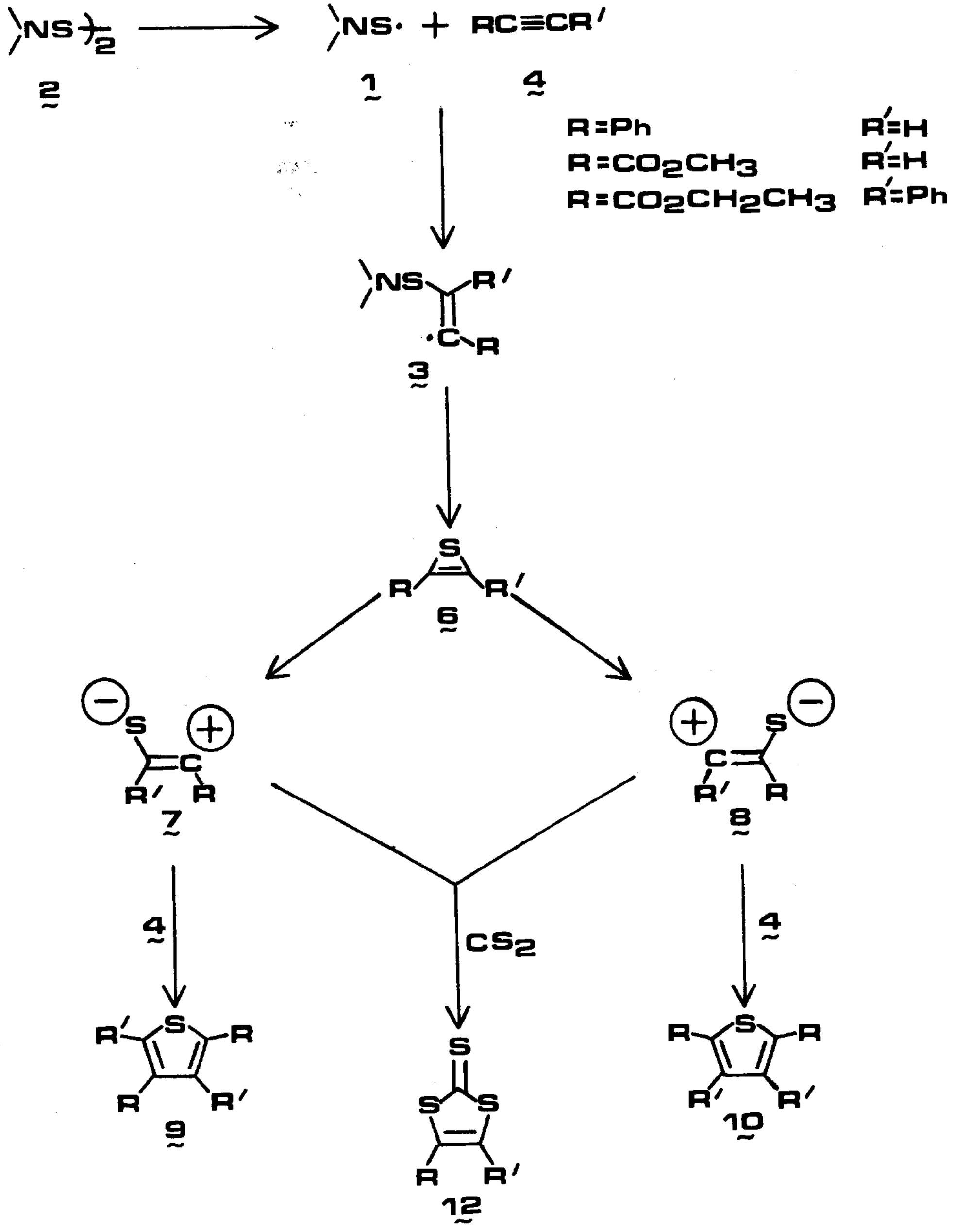
The reversible formation of thionitroxyl radicals 1 from the thermolysis of bis-amine disulfides 2 has been observed by esr spectroscopy[1,2]. These radicals are reputed to be relatively unreactive. We now report that bis-amine disulfides react regiospecifically with unsymmetrical acetylenes 4 to produce thiophenes, a reaction, which we propose is initiated by the addition of 1 to 4 to form a radical 3 as shown in Scheme I.

The predominant thiophene isomer depends on the R substituent in 4. Phenylacetylene (R=Ph) and morpholinodisulfide 5 gave 2,4-diphenylthiophene and 2,5-diphenylthiophene in a 3:1 ratio, while methyl propiolate ($R=CO_2CH_3$) and 5 formed dimethyl 2,5-thiophenedicarboxylate. (Table I). The reaction with ethyl phenylpropiolate and 5 was studied to determine which substituent, phenyl or $CO_2R$, controls the regiospecificity. The exclusive formation of diethyl 3, 4-diphenyl-2, 5-thiophenedicarboxylate demonstrates the dominance of the $CO_2R$ group. These last two reactions represent improved, convenient one step syntheses of compounds which were prepared by multi-step lower yield routes[3,4].

In order to explain the reversal in regiospecificity of thiophene formation, we propose a mechanism which involves the collapse of the radical 3 to a thiirene[5-7] 6. The fate of the nitrogen fragment is not clear as we have been unable to isolate non-polymeric nitrogen containing material.

The direction in which 6 opens to form the 1,3-dipoles 7 and 8 depends on R. When R is $CO_2R$, 6 will open to give 8. In this way the $CO_2R$ group is not substituted on a carbon which is electron deficient. However, when R is a phenyl-group, which will delocalize the positive charge in 7, 6 will open to produce 7 instead of 8. The dipoles 7 and 8 will react with more acetylene to generate the thiophenes 9 and 10, respectively[8].

# SCHEME I



)NS)2
2
)NS· + RC≡CR′
1
4
R=Ph R′=H
R=CO2CH3 R′=H
R=CO2CH2CH3 R′=Ph
3
6
7
8
4
CS2
4
9
12
10

Table I. Summary Of Products And Yields[a]

| 4 | | 2 | $CS_2$ | 9[b] | 10[b] | 12[c] | % Yield[d] |
|---|---|---|---|---|---|---|---|
| R=Ph | R′=H | 13 | no | 85 | 15 | — | 82 |
| R=Ph | R′=H | 13 | yes | 74 | 26 | 45 | 25 |
| R=Ph | R′=H | 5 | no | 74 | 26 | — | 52 |
| R=$CO_2CH_3$ | R′=H | 5 | no | 0 | 100 | — | 48 |
| R=$CO_2Et$ | R′=Ph | 5 | no | 0 | 100 | — | 67 |
| R=$CO_2Et$ | R′=Ph | 5 | yes | — | — | 99 | — |

a) experiments were conducted at 140° for 3 hours without $CS_2$ and 24 hours in a Parr bomb reactor with $CS_2$ at 140°, all compounds were identified by ms, nmr, ir, and comparison with known compounds where appropriate.

b) relative yields of thiophene isomers were determined by glpc.

c) isolated yield of 12 based on one atom of sulfur transfered from the disulfide.

d) isolated yield of 9 + 10 based on one atom of sulfur transfered from the disulfide.

In principle the dipole 8 can react with 4 to give 9 as well as 10 depending on which way the unsymmetrical acetylene orients with respect to 8. The formation of 10 to the exclusion of 9 can be understood in terms of frontier molecular orbital theory[9]. The dipole 8 may be viewed as having an empty 2p orbital which is located on the postively charged carbon and is perpendicular to the $\pi$-orbitals of the thioenolate. We propose that the reaction between 4 and 8 is initiated by the interaction of the empty 2p orbital of 8 with the $\pi$-HOMO of 4. The R′ carbon of 8 will become bonded to the R′ carbon of 4, giving rise to 10 rather than 9, because the coefficient for the atomic $2p\pi$ orbital located on the R′ carbon is larger than that for the R carbon in the HOMO of 4. The same argument holds for the reaction 7 + 4 → 9.

Dipoles 7 and 8 are known[10,11] to react with carbon disulfide 11 to give trithiocarbonates 12. When the reactions between 5 and ethyl phenylpropiolate, and between 2,2,6,6-tetramethylpiperidino-disulfide 13 and phenylacetylene were conducted with 11 present substantial amounts of 12 were produced as shown in Table I. The reaction represents a useful one step synthesis of trithiocarbonates which are intermediates in the preparation of tetrathiafulvalenes[12].

Two mechansims are ruled out by the formation of 10 from methyl propiolate and ethyl phenylpropiolate. First, the dimerization of 7 or 8 to form a 1,4-dithiin followed by elimination of sulfur will lead to exclusive production of 9. The addition of the radical 3 to 4 in the same direction as the addition of 1 to 4 will give a radical which will collapse to 9 only.

In summary, we have found a useful one step synthesis for thiophenes and trithiocarbonates. We propose that the regiospecificity in thiophene formation is due to the interaction between substituent R and the electron deficient carbon atom in the dipoles 7 and 8. Further experiments concerning the scope and limitations of the reactions will be presented later.

## References

1. W. C. Danen and D. D. Newkirk, J. Am. Chem. Soc., 98, 516 (1976).
2. B. Maillard and K. U. Ingold, ibid, 98, 520 (1976).
3. S. Oae, N. Furukawa, T. Watanabe, Y. Otsuji, and M. Hamata, Bull. Chem. Soc. Japan, 38, 1247 (1965).
4. H. J. Backer and W. Stevens, Rec. Trav. Chim., 59, 423 (1940).
5. O. P. Strausz, J. Font, E. L. Dedio, P. Kebarle, and H. E. Gunning, J. Am. Chem. Soc., 89, 4805 (1967).
6. M. J. S. Dewar and C. A. Ramsden, J. Chem. Soc. Chem. Comm., 688 (1973).
7. K. P. Zeller, H. Meier, and E. Müller, Tet. Let., 537 (1971).
8. L. Benati, P. C. Montevecchi, and G. Zanardi, J. Org. Chem., 43, 575 (1977).
9. K. N. Houk, Acc. Chem. Res., 8, 361 (1975).
10. R. Huisgen and V. Weberndorfer, Experientia, 17, 566 (1961).
11. S. Hunig and E. Fleckenstein, Ann, 138, 192 (1970).
12. H. D. Hartzler, J. Am. Chem. Soc., 92, 1412 (1970).